CLAIMS

1. A compound consisting of a total of 8-50 nucleotides and/or nucleotidee analogues, wherein said compound comprises a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located within a sequence selected from the group consisting of SEQ ID NO: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57.

2. A compound of according to claim 1, which modulates the expression of thioredoxin.

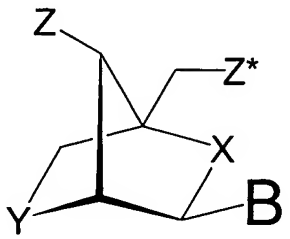
3. A compound of consisting of 8-50 nucleotides and/or nucleotidee analogues targeted to a nucleic acid molecule encoding TRX, wherein said compound specifically hybridises with a nucleic acid encoding TRX and inhibits the expression of TRX and wherein said compound comprises a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located within a sequence selected from SEQ ID NO: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, or 57.

4. The compound according to any of claims 1-3, which is an antisense oligonucleotide.

5. The compound according to any of claims 1-4, comprising at least one nucleotide analogue.

6. The compound according to any of claims 1-5, comprising at least one Locked Nucleic Acid (LNA) unit.

7. The compound according to claims 6, wherein the Locked Nucleic Acid (LNA) unit has the structure of the general formula



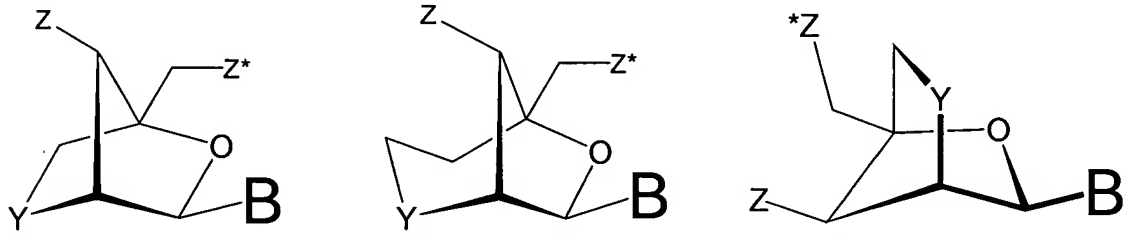
X and Y are independently selected among the groups -O-, -S-, -N(H)-, N(R)-, $-CH_2-$ or -CH- (if part of a double bond), $-CH_2-O-$, $-CH_2-S-$, $-CH_2-N(H)-$, $-CH_2-N(R)-$, $-CH_2-CH_2-$ or $-CH_2-CH-$ (if part of a double bond), -CH=CH-, where R is selected form hydrogen and C_{1-4}-alkyl ;

Z and Z* are independently absent, selected among an internucleoside linkage, a terminal group or a protecting group;

B constitutes a natural or non-natural nucleobase;

and the asymmetric groups may be found in either orientation.

8. The compound according to claim 6 or 7, wherein at least one nucleotide comprises a Locked Nucleic Acid (LNA) unit according any of the formulas



wherein Y is independently selected from -O-, -S-, -NH-, and $N(R^H)$;

Z and Z* are independently absent, selected among an internucleoside linkage, a terminal group or a protecting group; and

B constitutes a natural or non-natural nucleobase.

9. The compound according to any one of the preceding claims, wherein the nucleotide analogue comprises an internucleoside linkage selected from the group consisting of $-O-P(O)_2-O-$, $-O-P(O,S)-O-$, $-O-P(S)_2-O-$, $-S-P(O)_2-O-$, $-S-P(O,S)-O-$, $-S-P(S)_2-O-$, $-O-P(O)_2-S-$, $-O-P(O,S)-S-$, $-S-P(O)_2-S-$, $-O-PO(R^H)-O-$, $O-PO(OCH_3)-O-$, $-O-PO(NR^H)-O-$, $-O-PO(OCH_2CH_2S-R)-O-$, $-O-PO(BH_3)-O-$, $-O-PO(NHR^H)-O-$, $-O-P(O)_2-NR^H-$, $-NR^H-P(O)_2-O-$, $-NR^H-CO-O-$, where R^H is selected form hydrogen and C_{1-4}-alkyl.

10. The compound according to any one of the preceding claims, wherein the nucleotide analogue comprises a modified nucleobases selected from the group consisting of 5-methylcytosine, isocytosine, pseudoisocytosine, 5-bromouracil, 5-propynyluracil, 6-aminopurine, 2-aminopurine, inosine, diaminopurine, 2-chloro-6-aminopurine.

11. The compound according to any of claims 5-10, wherein the LNA is oxy-LNA, thio-LNA, amino-LNA in either the D-ß or L-α configurations or combinations thereof.

12. A compound consisting of a total of 8-50 nucleotides and/or nucleotidee analogues, targeted to a nucleic acid molecule encoding TRX, wherein said compound specifically hybridises with a nucleic acid encoding TRX and inhibits the expression of TRX and wherein said compound comprises a subsequence of at least 8 nucleotides or nucleotide analogues SEQ ID NO: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18.

13. The compound according to claim 4, wherein the antisense oligonucleotide is a design according to any of the designs presented in Figure 1.

14. The compound according to claim 13, wherein the antisense oligonucleotide is a gapmer.

15. The compound according to any of the claims 1-14, wherein the antisense oligonucleotide is a 13, 14, 15, 16, 17, 18, 19, 20 or 21-mer in lenght.

16. The compound according to any of the claims 1-15, comprising at least 2 LNA units, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 LNA units.

17. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 2a.

18. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 3a.

19. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 4a.

20. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 5a.

21. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 6a.

22. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 7a.

23. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 8a.

24. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 9a.

25. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 10a.

26. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 11a.

27. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 12a.

28. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 13a.

29. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 14a.

30. The compound according to any of the claims 1-16, wherein the subsequence is SEQ ID NO: 15a.

31. The compound according to any of claims 57-72, wherein the 3' end LNA is replaced by the corresponding natural nucleoside.

32. A compound consisting of SEQ ID NO: 2a.

33. A compound consisting of SEQ ID NO: 3a.

34. A compound consisting of SEQ ID NO: 4a.

35. A compound consisting of SEQ ID NO: 5a.

36. A compound consisting of SEQ ID NO: 6a.

37. A compound consisting of SEQ ID NO: 7a.

38. A compound consisting of SEQ ID NO: 8a.

39. A compound consisting of SEQ ID NO: 9a.

40. A compound consisting of SEQ ID NO: 10a.

41. A compound consisting of SEQ ID NO: 11a.

42. A compound consisting of SEQ ID NO: 12a.

43. A compound consisting of SEQ ID NO: 13a.

44. A compound consisting of SEQ ID NO: 14a.

45. A compound consisting of SEQ ID NO: 15a.

50. The compound according to any of claims 34-45, wherein the 3' end LNA is replaced by the corresponding nucleotide.

51. A conjugate comprising the compound according to any of claims 1-50 and at least one non-nucleotide or non-polynucleotide moiety covalently attached to said compound.

52. A pharmaceutical composition comprising a compound as defined in any of claims 1-51 or a conjugate as defined in claim 59, and a pharmaceutically acceptable diluent, carrier or adjuvant.

53. The pharmaceutical composition according to claim 51 further comprising at least one chemotherapeutic agent.

54. The pharmaceutical composition according to claim 52, wherein said chemotherapeutic compound is selected from the group consisting of adrenocorticosteroids, such as prednisone, dexamethasone or decadron; altretamine (hexalen, hexamethylmelamine (HMM)); amifostine (ethyol); aminoglutethimide (cytadren); amsacrine (M-AMSA); anastrozole (arimidex); androgens, such as testosterone; asparaginase (elspar); bacillus calmette-gurin; bicalutamide (casodex);

bleomycin (blenoxane); busulfan (myleran); carboplatin (paraplatin); carmustine (BCNU, BiCNU); chlorambucil (leukeran); chlorodeoxyadenosine (2-CDA, cladribine, leustatin); cisplatin (platinol); cytosine arabinoside (cytarabine); dacarbazine (DTIC); dactinomycin (actinomycin-D, cosmegen); daunorubicin (cerubidine); docetaxel (taxotere); doxorubicin (adriomycin); epirubicin; estramustine (emcyt); estrogens, such as diethylstilbestrol (DES); etopside (VP-16, VePesid, etopophos); fludarabine (fludara); flutamide (eulexin); 5-FUDR (floxuridine); 5-fluorouracil (5-FU); gemcitabine (gemzar); goserelin (zodalex); herceptin (trastuzumab); hydroxyurea (hydrea); idarubicin (idamycin); ifosfamide; IL-2 (proleukin, aldesleukin); interferon alpha (intron A, roferon A); irinotecan (camptosar); leuprolide (lupron); levamisole (ergamisole); lomustine (CCNU); mechlorathamine (mustargen, nitrogen mustard); melphalan (alkeran); mercaptopurine (purinethol, 6-MP); methotrexate (mexate); mitomycin-C (mutamucin); mitoxantrone (novantrone); octreotide (sandostatin); pentostatin (2-deoxycoformycin, nipent); plicamycin (mithramycin, mithracin); prorocarbazine (matulane); streptozocin; tamoxifin (nolvadex); taxol (paclitaxel); teniposide (vumon, VM-26); thiotepa; topotecan (hycamtin); tretinoin (vesanoid, all-trans retinoic acid); vinblastine (valban); vincristine (oncovin) and vinorelbine (navelbine).

55. A pharmaceutical composition comprising the compound of any of claims 1-50, which further comprises a pharmaceutically acceptable carrier.

56. A pharmaceutical composition comprising the compound of any of claims 1-50, which is employed in a pharmaceutically acceptable salt.

57. A pharmaceutical composition comprising the compound of any of claims 1-50, which is constitutes a pro-drug.

58. A pharmaceutical composition comprising the compound of any of claims 1-50, which further comprises an antiinflamatory compounds and/or antiviral compounds.

59. Use of a compound as defined in any of claims 1-50 or as conjugate as defined in claim 51 for the manufacture of a medicament for the treatment of cancer.

60. Use according to claim 59, wherein said cancer is in the form of a solid tumor.

61. Use according to claim 59 or 60, wherein said cancer is a carcinoma.

62. Use according to claim 61, wherein said carcinoma is selected from the group consisting of malignant melanoma, basal cell carcinoma, ovarian carcinoma, breast carcinoma, non-small cell lung cancer, renal cell carcinoma, bladder carcinoma, recurrent superficial bladder cancer, stomach carcinoma, prostatic carcinoma, pancreatic carcinoma, lung carcinoma, cervical carcinoma, cervical dysplasia, laryngeal papillomatosis, colon carcinoma, colorectal carcinoma and carcinoid tumors.

63. Use according to claim 62 wherein said carcinoma is selected from the group consisting of malignant melanoma, non-small cell lung cancer, breast carcinoma, colon carcinoma and renal cell carcinoma.

64. Use according to claim 63, wherein said malignant melanoma is selected from the group consisting of superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral melagnoma, amelanotic melanoma and desmoplastic melanoma.

65. Use according to claim 60 or 61, wherein said cancer is a sarcoma.

66. Use according to claim 65, wherein said sarcoma is selected from the group consisting of osteosarcoma, Ewing's sarcoma, chondrosarcoma, malignant fibrous histiocytoma, fibrosarcoma and Kaposi's sarcoma.

67. Use according to claim 60 or 61, wherein said cancer is a glioma.

68. A method for treating cancer, said method comprising administering a compound as defined in any of claims 1-50, a conjugate as defined in claim 51 or a pharmaceutical composition as defined in any of claims 52-58 to a patient in need thereof.

69. The method according to claim 68, wherein said cancer is in the form of a solid tumor.

70. The method according to claim 68 or 69, wherein said cancer is a carcinoma.

71. The method according to claim 70, wherein said carcinoma is selected from the group consisting of malignant melanoma, basal cell carcinoma, ovarian carcinoma, breast carcinoma, non-small cell lung cancer, renal cell carcinoma, bladder carcinoma, recurrent superficial bladder cancer, stomach carcinoma, prostatic carcinoma, pancreatic

carcinoma, lung carcinoma, cervical carcinoma, cervical dysplasia, laryngeal papillomatosis, colon carcinoma, colorectal carcinoma and carcinoid tumors.

72. The method according to claim 71, wherein said carcinoma is selected from the group consisting of malignant melanoma, non-small cell lung cancer, breast carcinoma, colon carcinoma and renal cell carcinoma.

73. The method according to claim 124, wherein said malignant melanoma is selected from the group consisting of superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral melagnoma, amelanotic melanoma and desmoplastic melanoma.

74. The method according to claim 68, wherein said cancer is a sarcoma.

75. The method according to claim 74, wherein said sarcoma is selected from the group consisting of osteosarcoma, Ewing's sarcoma, chondrosarcoma, malignant fibrous histiocytoma, fibrosarcoma, artherosclerosis, psoriasis, diabetic retinopathy, rheumatoid arthritis, asthma, warts, allergic dermatitis and Kaposi's sarcoma.

75. The method according to claim 68, wherein said cancer is a glioma.

76. A method of inhibiting the expression of TRX, in cells or tissues comprising contacting said cells or tissues with the compound according to any of claims 1-50 so that expression of TRX is inhibited.

77. A method of modulating expression of a gene involved in a cancer disease comprising contacting the gene or RNA from the gene with an oligomeric compound wherein said compound has a sequence comprising at least an 8 nucleobase portion of SEQ ID NO: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57 whereby gene expression is modulated.

78. A method according to claim 77, wherein the compounds comprises one or more LNA units.

79. The method of claim 77 or 78, wherein the compound hybridizes with messenger RNA of the gene to inhibit expression thereof.

80. A method of treating a mammal suffering from or susceptible from an cancer disease, comprising:
administering to the mammal an therapeutically effective amount of an oligonucleotide targeted to TRX that comprises one or more LNA units.

81. The method according to any of the claims 77-80, wherein the cancer diseases is a lung, breast, colon, prostate, pancreas, lung, liver, thyroid, kidney, brain, testes, stomach, intestine, bowel, spinal cord, sinuses, bladder, urinary tract or ovaries cancer.

82. A method of modulating the red blood cell proliferation, cellular proliferation, ion metabolism, glucose and energy metabolism, pH regulation or matrix metabolism comprising contacting a cell with the antisense compound of claim 1-50 so that the cell is modulated.

83. A method of inhibiting the proliferation of cells comprising contacting cells in vitro with an effective amount of the antisense compound of claim 1-50, so that proliferation of the cells is inhibited.

84. The method of claim 83 wherein said cells are cancer cells.

85. A method of inhibiting the expression of TRX in human cells or tissues comprising contacting human cells or tissues with the compound of claim 1-50 so that expression of TRX is inhibited.

86. A method of treating an animal having a disease or condition associated with TRX comprising administering to an animal having a disease or condition associated with TRX a therapeutically or prophylactically effective amount of the antisense compound of claim 1 so that expression of TRX is inhibited.

87. The method of claim 86 wherein the disease or condition is a hyperproliferative condition.

88. The method of claim 87 wherein the hyperproliferative condition is cancer.

89. A method of treating a human having a disease or condition characterized by a reduction in apoptosis comprising administering to a human having a disease or condition

characterized by a reduction in apoptosis a prophylactically or therapeutically effective amount of the antisense compound of claim 1-50.

90. A method of modulating apoptosis in a cell comprising contacting a cell with the antisense compound of claim 1-50 so that apoptosis is modulated.

91. A method of modulating cytokinesis in a cell comprising contacting a cell with the antisense compound of claim 1-50 so that cytokinesis is modulated.

92. A method of modulating the cell cycle in a cell comprising contacting a cell with the antisense compound of claim 1-50 so that the cell cycle is modulated.

93. A method of inhibiting the proliferation of cells comprising contacting cells with an effective amount of the antisense compound of claim 1-50, so that proliferation of the cells is inhibited.